

Sub 23
21. An autoclavable composition of an aqueous injectable terminally steam sterilized suspension in a vial sealed under nitrogen atmosphere, said suspension containing particles of a water insoluble or poorly soluble biologically active substance with a volume weighted mean particle size of up to 3 μm with not more than 3000 particles of 10 μm or greater size and not more than 300 particles of 25 μm or greater size, said particles surface stabilized with one or more phospholipid surface modifier, and a pharmaceutically acceptable amount safe for parenteral administration of a pharmaceutically acceptable, water soluble polyhydroxy thermoprotecting agent selected from the group consisting of one or a combination of trehalose, lactose, dextrose, sorbitol, dextran, trehalose and mannitol, wherein the pH of said suspension is between 5 to 9, the ratio of said active substance to said surface modifier is 1:1 to 5:1, and the amount of said surface modifier is in the range from 0.2% w/w to 5.0% w/w, wherein said composition is substantially completely devoid of surfactants that require during terminal steam sterilization elevation of their cloud point temperature by addition of a cloud point modifier, said composition is substantially devoid of surfactant additives which coagulate on steam sterilization, and said volume weighted mean particle size is not increased more than two-fold during and after terminal steam sterilization.

22. An autoclavable composition of an injectable non-flocculating aqueous terminally steam sterilized suspension under nitrogen in a sealed vial, said suspension containing particles of a water insoluble or poorly soluble drug substance with a volume weighted mean particle size of up to 3 μm with not more than 3000 particles of 10 μm or greater size and not more than 300 particles of 25 μm or greater size, said particles surface stabilized with one or more phospholipid surface modifier, and a pharmaceutically acceptable amount safe for parenteral administration of

DIFF -
No 3rd Rpt

a pharmaceutically acceptable, water soluble polyhydroxy thermoprotecting agent, wherein the pH of said suspension is between 5 to 9, the ratio of said drug to said surface modifier is 1:1 to 5:1, the amount of said surface modifier is in the range from 0.2% w/w to 5.0% w/w, and said volume weighted mean particle size is not increased more than two-fold during and after terminal steam sterilization, and wherein said composition is substantially completely devoid of surfactants that require during terminal steam sterilization elevation of their cloud point temperature by addition of a cloud point modifier and substantially devoid of surfactant additives which coagulate on steam sterilization.

23. The composition of claim 21 or claim 22, wherein the suspension also includes an amount of non-surfactant additives such that the suspension attains an osmotic pressure safe for parenteral administration.

24. The composition of claim 21 or claim 22, wherein the suspension can be diluted with water for parenteral administration.

25. The composition of claim 22, wherein the polyhydroxy compound is selected from the group consisting of one or a combination of trehalose, lactose, dextrose, sorbitol, dextran, trehalose and mannitol.

26. The composition of claim 21 or claim 22, wherein the phospholipid surface modifier is selected from the group consisting of natural phospholipids and synthetic phospholipids.

27. The composition of claim 26 wherein the natural phospholipid is an egg phospholipid or soy phospholipid.

28. The composition of claim 22, wherein the suspension also contains pharmaceutical excipients for ophthalmic, peroral, or transdermal administration of the water insoluble or poorly soluble active drug substance.

29. The composition of claim 21, wherein the active substance is an antifungal agent.

30. The composition of claim 29, wherein the antifungal agent is itraconazole.

11 31. The composition of claim 21, wherein the active substance is an immunosuppressive agent.

32 33. The composition of claim 21, wherein the active substance is a sterol.

33 34. The composition of claim 33, wherein the sterol is alfaxalone.

34 35. A lyophilized or spray dried powder prepared from the composition of claim 22.

35 36. A composition according to claim 22, wherein the water-insoluble or poorly water-soluble drug substance is suitable for either immediate release or sustained release delivery of said drug substance by parenteral administration.

36 37. The composition of claim 36 wherein the parenteral administration is intramuscular, or subcutaneous administration.